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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/319,156	11/02/1999	GLAUCIA PARANHOS-BACCALA	103514	2490

25944 7590 02/07/2007

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/319,156	PARANHOS-BACCALA ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,9,14,15,26,28-30,36-38,40-42,45-47,49-51 and 60-66* is/are pending in the application.

4a) Of the above claim(s) *26* is/are withdrawn from consideration.

5)☒ Claim(s) *65 and 66* is/are allowed.

6)☒ Claim(s) *1,7,9,14,15,26,28-30,36-38,40-42,45-47,49-51 and 60-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 November, 2005,* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Supplemental Office Action

Status of the Claims

Applicants' representative requested clarification concerning the claim status during a personal interview conducted on 20 July, 2006. Accordingly, the following supplemental office action is being provided to clarify the last action. Claims 1, 7, 9, 14, 15, 26, 28-30, 36-38, 40-42, 45-47, 49-51, and 60-66 are pending in the instant application. Claim 26 stands withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention (see the restriction requirement mailed 16 February, 2001). Applicants' request that this claim be rejoined upon the identification of allowable subject matter is noted. Claims 1, 7, 9, 14, 15, 28-30, 36-38, 40-42, 45-47, 49-51, and 60-66 are currently under examination.

37 C.F.R. § 1.84

Acknowledgement is hereby made of receipt and entry of the drawings filed on 07 November, 2005, which are deemed to be acceptable.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 14, 15, 28-30, 36-38, 45-47, 49-51, and 60-64 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claims are confusing for referencing polynucleotides comprising a nucleic acid having a nucleotide sequence selected from the recited sequences. It is not readily manifest if applicants are attempting to claim portions of these sequences (i.e., dimers or greater) or the full-length sequences themselves. Appropriate correction is required (i.e., An isolated polynucleotide comprising one of the full-length sequences set forth in SEQ ID NO.: 6, 9, or 12; An isolated polynucleotide comprising one of the full-length sequences, or a portion thereof, set forth in SEQ ID NO.: 6, 9, or 12).

The claims also reference the term "contiguous monomers" which is confusing. The term monomer generally refers to a small molecule that is linked with large numbers of other small molecules to form a chain or a network (polymer).[1] Polynucleotides are multimeric or polymeric structures, not monomeric structures. It is suggested that applicants amend the claim language to recite --nucleotides-- (i.e., sequences that display 70% genetic relatedness along each stretch of 100 contiguous nucleotides).

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most

1 See http://antoine.frostburg.edu/chem/senese/101/glossary/m.shtml, http://www.dddmag.com/Glossary.html?RPTID=KWSRCH&SEARCHWORD=monomer&SEARCHMETHOD=WORD, and http://www.biology-online.org/dictionary/Monomer for art-recognized definitions of the term.

nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1, 7, 9, 14, 15, 28-30, 36-38, 40-42, 45-47, and 60-64 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398, (Fed. Cir. 1997). *Fiers v. Revel Co.*, 984 F.2d 1164, 25 U.S.P.Q.2d 1601, (Fed. Cir. 1993). *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016, (Fed. Cir. 1991). *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 U.S.P.Q.2d 1609, (Fed. Cir. 2002). *Univ. of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 920, 69 U.S.P.Q.2d 1886, (Fed. Cir. 2004). *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *University of Rochester* v. *G. D. Searle & Co., Inc.*, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004).

The claims are directed toward various nucleotide sequences that share 70%, 80%, 90%, and 95% genetic relatedness to the parent sequences for every 100 nucleotides. Thus, the limitations only apply to as little as a portion of each nucleotide sequence. As previously set forth, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for

the broadly claimed genus of nucleic acids.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "**laundry list**" disclosure of every possible moiety does **not** constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant

identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

Moreover, where claims directed toward nucleic acids are concerned, legal precedence also clearly dictates that conception of a chemical compound (e.g., a DNA molecule) is not achieved until reduction to practice has occurred (*University of California* v. *Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016-1031

(C.A.F.C. 1991); *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993); *In re Bell*, 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993); *In re Deuel*, 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995)). In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* the court concluded that "It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated." The significance of conception and reduction to practice was further addressed by the court in *Fiers v. Sugano* where it was emphasized that "Conception is a question of law, reviewed *de novo* on appeal, and if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated; thus, regardless of complexity or simplicity of method of isolation employed, conception of DNA sequence, like conception of any chemical substance, requires definition of that substance other than by its functional utility." Thus, the courts have emphasized that the inventor must clearly and unambiguously identify the salient characteristics and properties of any given claimed nucleotide sequence. It is not sufficient to provide a vague reference to the biological activity of any given nucleotide sequence or some generic method of obtaining it.

The disclosure describes the isolation and characterization of a novel human retrovirus that may be associated with multiple sclerosis. A molecular clone was obtained and the purported

nucleotide sequence of the *env* gene ascertained. Thus, the skilled artisan would reasonably conclude that applicants were in possession of those particular clones containing SEQ ID NOS.: 6, 9, and 12. Appropriately drafted claim language directed toward these embodiments would be acceptable. However, the broadly recited claim language directed toward fragments, equivalents, and homologous sequences is unacceptable. The sequences of interest are 635 nt, 1481 nt, and 1329 nt in length (SEQ ID NOS.: 6, 9, and 12, respectively). The claims only stipulate that these sequences have the recited genetic relatedness (e.g., 70%, 80%, 90%, and 95%) for every stretch of 100 nucleotides. Thus, for each of the identified sequences as many as 535 nt, 1381 nt, and 1229 nt do not require any particular structural information. This genus of variants encompasses an inordinate number of species. For instance, if the degree of genetic relatedness is extended to the full-length sequences (not just a 100 nt stretch), at 70% genetic relatedness sequence six would encompass 9×10^{260} variants, sequence nine 9×10^{606} variants, and sequence 12 2×10^{544} variants. Even if the degree of genetic relatedness is extended to 95%, the claims would still encompass the following number of variants for each sequence: 9×10^{71}, 6×10^{164}, and 2×10^{147}, respectively.[2] The disclosure only provides nucleotide sequence data from a single MSRV isolate. Moreover, the disclosure fails to identify any critical molecular determinants modulating the functional activities of the Env glycoprotein. It has been well-documented in the prior art that single or multiple amino acid substitutions, addtions, or deletions can have profound influences on protein activity. Therefore, the skilled artisan has been asked to guess as to which of the various nucleic acids might retain the

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2 These calculations were based upon the following equation: $(3^n * sl!)/(n! * sl-n-1)$. n equals the number of nucleotides that can be substituted and sl equals the sequence length of interest.

desired activity. Finally, perusal of the specification fails to lead the skilled artisan to any particular sequence.

Furthermore, the court concluded in *In re Gosteli* that the disclosure of a single species is insufficient support for claims directed toward a broader genus. *In re Gosteli*, 872 F.2d 1008, 1010, 10 U.S.P.Q.2d 1614, 1616 (Fed. Cir. 1989). The importance of providing detailed structural information for a representative number of species was also emphasized by the court in *Univ. of Rochester* who stated that the disclosure contained in the application "just represents a wish, or arguably a plan, for obtaining the DNA," and that "it does not indicate that [the applicant] was in possession of the DNA." *Id.* at 1171. The court added that **a description of DNA requires "a precise definition, such as by structure, formula, chemical name, or physical properties...."** As referenced above, the court said that "[c]laiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived." *University of Rochester* v. *G.D. Searle & Co.*, 68 U.S.P.Q.2d 1424 (D.C. W.N.Y. 2003)

Applicants traverse and submit that the disclosure provides an adequate written description of the claimed invention. Applicants further attempt to distinguish themselves from the case law relied upon. While the written description requirement needs to be applied on a case-by-case basis, nevertheless, the requirements are still the same. There needs to be a structural/functional nexus that allows the skilled artisan to reasonably envisage those molecules that are currently being claimed. The disclosure is deficient in this attempt as set forth in rejection *supra*. Simply providing a nucleotide sequence in the absence of further identification of the molecular determinants modulating the desired properties of said sequence is insufficient to put the entire genus

of claimed variants within the possession of applicants. Accordingly, the rejection is proper and hereby maintained.

35 U.S.C. § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 14, 15, and 60 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Boehringer Mannheim (1994). The claims encompass as few as two nucleotides. The Boehringer Mannheim publication discloses DNA labeling kits comprising a mixture of hexanucleotides that contains all possible six-nucleotide sequences. Accordingly, this teaching meets all of the claimed limitations.

Allowable Subject Matter

Claims 65 and 66 appear to be free of the prior art and are allowable.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

31 January, 2007